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10/566,112	07/09/2007	Jianqing Chen	57637/1062	9580

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EXAMINER	
JONES, DAMERON LEVEST	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
12/28/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

klpatent@kramerlevin.com

Office Action Summary	Application No.	Applicant(s)	
	10/566,112	CHEN ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/12/10; 6/3/09; and 1/24/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *157-221 and 223-230* is/are pending in the application.

4a) Of the above claim(s) *157-192, 195-213, 216, 218, 230 (in part)* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *193, 194, 214, 215, 219-229, and 230 (in part)* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/10; 9/18/8; and 3/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 10/12/10 wherein claims 1-156 were canceled and claims 214-230 were added. In addition, the Examiner acknowledges receipt of the amendments filed 6/3/09 and 1/24/06.

Notes: (1) Claims 157-221 and 223-230 are pending.

(2) It is duly noted that while there is a listing for claim 222, there is no text that appears beside the number. Thus, the actual status of that claim is unclear.

APPLICANT'S INVENTION

2. The instant invention is directed to radiopharmaceuticals compositions and uses thereof as set forth in claims 157, 158, 159, 160, 161, 164, 175, 182, 189, 190, 193, 196, 197, 198, 20, 203, 206, 210, 214, 215, 216, 217, 218, and 230.

RESPONSE TO APPLICANT'S ELECTION

3. Applicant's election with traverse of Group VI filed 10/12/10 is acknowledged. The traversal is on the ground(s) that each of Groups I – IV are directed to stabilizing compositions (a detailed discussion is found below). Applicant's traversal is found non-persuasive. It is noted that only Groups I-IV were traversed; therefore; the remaining Groups V - IX have been viewed as an election without traverse.

It is duly noted in Applicant's response filed 10/12/10 initially Applicant elected Group VI for prosecution without traverse (see first complete paragraph on page 24). However, later in Applicant's response (page 25, first complete paragraph), it was stated that the election was with traverse. The traversal is on the basis that each of the groups requires a radiopharmaceutical composition, stabilizer, radionuclide, chelator,

and targeting molecule. Thus, Applicant asserts that each of the claims is directed to structurally similar radiopharmaceutical compositions. Furthermore, it is asserted that the Examiner misunderstands the invention since the restriction address stabilizers having one non-alpha amino acid with a cyclic group or at leas one bile acid. Applicant asserts that since the groups are directed to stabilized compositions, the inventions disclosed overlapping subject matter.

Applicant's assertions are not persuasive for the reasons set forth below. For example, Groups I – IV are distinct because the components present in the composition are non-obvious variants of one another. Group I unlike Groups II, III, and IV does not require a chelator (see independent claim 157), targeting agent, bile acid, or non-alpha amino acid with a cyclic group. Group II unlike Groups III and IV does not require the presence of at least one non-alpha amino with a cyclic group or at least one bile acid. Group III unlike Group IV requires at least one non-alpha amino acid with a cyclic group instead of at least one bile acid. Thus, while the groups are directed to radiopharmaceutical compositions, the components of the compositions are not obvious variants of one another. Therefore, a search of one group would not render obvious the other groups. In support of the Examiner's position, Applicant's attention is directed to the rejection made of record below. What the rejection illustrates is that one may have a composition comprising a radionuclide and stabilizer, but not render obvious a composition having additional components such as a targeting agent, a chelator, a bile acid, or a non-alpha amino acid with a cyclic group. Hence, the restriction is deemed proper and is made **FINAL**.

Notes: (1) It is noted that Applicant elected the species of claim 217. Initially, Applicant's elected species was searched. However, since no prior art was cited that could be used to reject the instant invention, the search was expanded to the species disclosed in Liu et al (US 2002/0122768) and Gustafson et al (British Journal of Industrial Medicine, 1985, Vol. 42, page 591-595). The search was not further expanded because prior art was found which could be used to reject the claims.

(2) In Applicant's election filed 10/12/10, page 25 (end of the first complete paragraph), it is stated that the elected species reads on claims 193, 194, and newly added claims 214-229. The statement is incorrect because Applicant elected the species of claim 217. The species of claim 217 does not contain a substituted bile acid. Instead, it contains two non-alpha amino acids with cyclic groups. Therefore, the elected species cannot read on claims 216 and 218. Thus, claims 193, 194, 214, 215, 217, and 219-230 read on the elected species.

WITHDRAWN CLAIMS

4. Claims 157-192, 195-213, 216, and 218 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention/species.

Notes: Claims 157-192, 195-213, and 230 (in part) are directed to the non-elected invention. Claims 216 and 218 are directed to the non-elected species.

112 FIRST PARAGRAPH REJECTION

Written Description Rejection

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 193, 194, 214, 215, 217, and 219-230 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is reminded that an Inventor is entitled to a patent to protect his work only if he/she produces or has possession of something truly new and novel. The invention being claimed must be sufficiently concrete so that it can be described for the world to appreciate the specific nature of the work that sets it apart from what was before. The Inventor must be able to describe the item to be patented with such clarity that the Reader is assured that the Inventor actually has possession and knowledge of the unique composition that makes it worthy of patent protection. The instant application does not sufficiently describe the invention as it relates to the reaction reactants and products that are compatible with the instant invention. Specifically, one cannot ascertain if Applicant's invention will work with ALL reactions that produce a radiopharmaceutical. In additon, Applicant is reminded that while a generic claim may define the boundaries of a vast genus of radiopharmaceuticals, the question may still remain as to whether or not the specification, including original claim language, demonstrates that Applicant has invented species sufficient to support a claim to a genus. In this particular instance, the problem is especially acute since the claims are directed to a desired result without describing the reactants without describing species

that achieved the desired result. What the Reader gathers from the instant application is a desire/plan/first step for obtaining a desired result. While the Reader can certainly appreciate the desire for achieving a certain end result, establishing goals does not necessarily mean that an invention has been adequately described.

While compliance with the written description requirements must be determined on a case-by-case basis, the real issue here is simply whether an adequate description is necessary to practice an invention described only in terms of its function and/or based on a disclosure wherein a description of the components necessary in order for the invention to function are lacking. In order to satisfy the written description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the Inventor possessed the claimed invention at the time of filing. In other words, the specification should describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that the Inventor created what is the claimed. Thus, the written description requirement is lacking in the instant invention since the various terms as set forth above are not described in a manner to clearly allow persons of ordinary skill in the art to recognize that Applicant invented what is being claimed.

Essential Subject Matter Missing

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 228-230 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The phrase 'water soluble organic compound containing selenium +2' is critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

The claims (i.e., claims 228, 229, and 230 which depend on claim 228) incorporated the phrase 'water soluble organic compound' into the claims. However, the specification does not provide support for the claim. Review of the specification (i.e., paragraph [0365] of the published application US 2002/0122768) indicates that the phrase 'water soluble aromatic amine' is present in the specification, not 'water soluble organic compound'. But, it is duly noted that in the application as originally filed, the phrase 'water soluble organic compound containing selenium +2' is present in the claims. Hence, Applicant is respectfully requested to incorporate the necessary phrases in the specification since they are present in the originally filed claims.

112 SECOND PARAGRAPH REJECTIONS

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 193, 194, 214, 215, 217, and 219-230 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 193, 194, 214, 215, 217, and 219-230: The claims as written are ambiguous because it is unclear what reactants are present in the reactions. In additon,

it is unclear if Applicant is claiming that the instant invention will work in ALL reactions that produce a radiopharmaceutical composition in the presence of benzyl alcohol.

Claims 193, 194, 214, 215, 217, and 219-230: The phrase "increasing recovery" in independent claim 193 is a relative phrase which renders the claims indefinite. The term "increasing recovery" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In particular, it is unclear what the radioactivity recovery is being compared to in order to determine whether or not an increase is actually present. Also, how one defines the term 'increase' varies from person to person, it is unclear what guidelines Applicant has established that must be met in order to truly determine if an increase in radioactivity is truly present.

Claims 221, 223, 224, 226, and 229: The claims as written are ambiguous because of the phrases 'analogs and derivatives thereof', 'analog thereof', and 'derivatives thereof'. In particular, the claim is ambiguous because it is unclear what portion of the parent structures are present in the analogs and derivatives that Applicant is claiming. In additon, it is not clear how Applicant how one is distinguishing between an analog and a derivative of the peptides listed in claim 221.

Claim 225: The claims as written are ambiguous because it is unclear what GRP agonist or peptide Applicant is claiming that confer agonist activity to the desired molecule.

Claim 222: The claim as written is ambiguous. In particular, it is noted that while it appears that Applicant is adding claim 222, there is no claim status or text that appears after '222.'. Please make the appropriate corrections.

Claim 228: The claims as written are ambiguous because it is unclear what specific water soluble organic compounds Applicant is claiming that are compatible with the instant invention and that yield the desired results.

102 REJECTION

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claim 193 is rejected under 35 U.S.C. 102(b) as being anticipated by Gustafson et al (British Journal of Industrial Medicine, 1985, Vol. 42, pages 591-595).

Gustafson et al disclose the influences of organic solvent mixtures on biological membranes (see entire document, especially, abstract; page 592-593, 'Influence of Solvents on Membrane Integrity'; pages 594-595, bridging paragraph). In particular, Table 3 (page 594) discloses release radioactivity in benzyl alcohol alone and benzyl alcohol and ethanol . The released radioactivity of benzyl alcohol is disclosed at 5.0 $\pm$ 3.7 and benzyl alcohol and ethanol is 50.9 $\pm$ 9.3. Thus, both Applicant and Gustafson et al disclose an increase of radioactivity recovery resulting from a radiopharmaceutical composition reaction.

103 REJECTION

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 193, 194, 214, 215, and 219-228 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al (US 2002/0122768).

Liu et al disclose stable radiopharmaceutical compositions of methods of preparing the compositions. The compositions comprise a radionuclide and an effective stabilizing amount of an aromatic stabilizer that may be used alone or in combination with other stabilizers. The purpose of the stabilizer is to inhibit radiolytic degradation of the radiopharmaceutical (see entire document, especially, abstract; page 3, paragraph [0035]; pages 3-4, paragraph [0036]). The radiopharmaceutical agents may comprise a chelating agent, radionuclide, linking group, and a biological molecule/targeting agent (page 4, paragraphs [0037] – [0069]). Possible stabilizers that may be used alone or in combination include benzyl alcohol and ascorbic acid (page 4, paragraph [0053]; page 5, paragraph [0070]; page 6, paragraph [0098]; page 20, paragraphs [0360] – [0364]). Possible metal chelators include DTPA, DOTA, DO3A, and other cyclic and acyclic polyaminocarboxylates (page 16, paragraphs [0314] – [0315]). Suitable radionuclides include selenium-75, technetium-99m, gallium-67, scandium-47, copper-64, and gold-199 (page 17, paragraphs [0321] and [0322]). Various biomolecules ranging from EGF, interleukin, interferon, luteinizing hormone releasing factor to other proteins, antibodies, antibody fragments, peptides, polypeptides, or peptidomimetics (pages 18-20, [0338] - [0355]; page 21, paragraph [0372]). In addition, Liu et al disclose Compound A (pages 23-26, paragraphs [0404] – [0420] and Compound C (pages 32 - 36, paragraph [0449] – [0458]), for example, disclose compounds having a targeting agent, chelator, radionuclide, and linker. Thus, a skilled artisan would recognize that radioactivity from the radiopharmaceutical composition reaction would increase because radiolytic degradation of the radiopharmaceutical is inhibited (see abstract; page 9, paragraph

[0134]). Hence, both Applicant and Gustafson et al disclose an increase of radioactivity recovery resulting from a radiopharmaceutical composition reaction.

SPECIFICATION

17. The disclosure is objected to because of the following informalities: on page 48, lines 6, 13, 19, 25, and 31, there are question marks before the wavelength. Did Applicant intend to correct/remove the information?.

Appropriate correction is required.

COMMENTS/NOTES

18. It should be noted that Applicant's elected invention was interpreted as the amount of radioactivity of the radiopharmaceutical increases anytime benzyl alcohol is present in the mixture.

19. It should be noted that while the Examiner indicated that no prior art was cited against Applicant's elected species (the species of claim 217), Applicant still MUST address and overcome the 112 rejections below. In particular, the prior art neither anticipates nor renders obvious Applicant's elected species.

20. In claim 217, line 1, Applicant is respectfully requested to correct the spelling of 'radiopharmaceutical' in the claim.

21. In claim 227, line 1, Applicant is respectfully requested to correct the spelling of 'method' in the claim.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571)272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/D. L. Jones/
Primary Examiner
Art Unit 1618

December 17, 2010